UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,857	01/31/2007	Ainara Vallejo Illarramendi	020884-000007	1371

24239 7590 01/14/2009

MOORE & VAN ALLEN PLLC
P.O. BOX 13706
Research Triangle Park, NC 27709

EXAMINER	
MACFARLANE, STACEY NEE	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
01/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,857	ILLARRAMENDI ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17 and 19-27* is/are pending in the application.

4a) Of the above claim(s) *1-15,17 and 22-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-15, 17 and 19-27 are pending in the instant application. Applicant's election of Group VI, claims 19-21 in so far as they are drawn to a method for the treatment of demyelinating diseases comprising administration of a DUSP6 protein antagonist compound, in the reply filed on May 12, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-15, 17 and 22-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 12, 2008.

3. Claims 19-21, in so far as they are drawn to a method for the treatment of demyelinating diseases comprising administration of a DUSP6 protein antagonist compound that inhibits DUSP6 protein expression and/or activity, will be examined upon their merits in the instant Office action.

Claim Objections

4. Claim 20 is objected to for reciting subject matter that is not elected for prosecution upon the merits.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is vague and indefinite in so far as it employs the term "DUSP6" as a limitation. This term appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "DUSP6". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "DUSP6", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

7. Claims 20 and 21 are indefinite for depending from an indefinite claim.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites "DUSP6 protein antagonists". Claims 20 and 21 are dependent from Claim 1 and do not further limit the "DUSP6 protein antagonists", and are therefore included in the rejection. The claims do not require that the "DUSP6 protein antagonists" possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules that is defined merely by the functions that it serves (e.g. "inhibits DUSP6 protein expression" or "inhibiting one or more DUSP6 protein functions") and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is not clear that Applicant is in possession of any specific examples of DUSP6 protein antagonists (paragraph [0079]). The claims, however, encompass method of administration of "DUSP6 protein antagonists", thus, the claims are not limited to specific molecules with known structure and merely require the claimed methods employ molecules that serve to inhibit DUSP6 expression or function.

In order to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional

characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of activity. The instant specification does not identify any particular portion of a structure that must be conserved for said activity. As stated above, it is not even clear what molecules are encompassed within the genus of DUSP6 protein antagonists. The specification does not provide a complete structure of either or those antagonists described therein and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the required genus of antagonistic compounds.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of DUSP6 protein antagonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v*

Revel, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims are drawn to a method for treatment of neurodegenerative phase of demyelinating diseases comprising administration of an agent that inhibits DUSP6 protein expression and/or activity.

Claims 19-21 broadly encompass methods of treatment of any demyelinating disease by the administration of any DUSP6 protein antagonist. Thus, the claims are

broadly drawn to methods for the treatment of a vast array of demyelinating diseases, including genetically inherited or congenital demyelinating disorders such as Charcot-Marie-Tooth, comprising the administration of *any* agent that inhibits DUSP6 protein expression and/or activity.

The invention is based on the following findings: microarray analysis demonstrates differential expression of *dusp6* gene in oligodendrocytes upon stimulation with AMPA versus control; dusp6 antisense oligonucleotides inhibits cell death of oligodendrocytes; and elevated expression of Dusp6 in post-mortem tissue from Multiple Sclerosis patients. However, the instant specification provides neither enough guidance, nor working examples, which would show that the claimed method comprising inhibition of DUSP6 protein expression and/or activity by a protein antagonist is effective to treat any demyelinating disease. Absent such guidance, one of ordinary skill in the art would require undue experimentation to discover how to practice Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The current state of the art recognizes that DUSP6 regulates more than one MAPK pathway and functions in “a complex negative regulatory network in which

individual MAPK activities can be subject to negative feedback control" (Owens et al., Oncogene, 26:3203-3213, May 2007). The reference goes on to point out that the catalytic domain of DUSP6 alone has very low phosphatase activity, and that its activity is largely dependent upon its interaction with other signaling molecules such as ERK. The Owens reference also suggests that DUSP6 may function downstream of more than one FGF receptor and that there is considerable redundancy in these pathways but that future studies and generation of knockout models will serve to further elucidate DUSP6 function in both normal physiology and disease. Taken together, the lack of guidance within the specification as to how the method of treating a demyelinating disease comprising administration of a DUSP6 protein antagonist, and the teachings within the current art that indicate the function of DUSP6 remains largely unknown, indicates that, at the time of filing, much unpredictability remained within the art with respect to a nexus between DUSP6 function and the underlying pathology of any demyelinating disease.

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be given their broadest reasonable interpretation that is consistent with the specification. See MPEP 2111 [R-1], which states: "During patent examination, the pending claims must be "given [their] broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always

has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the claimed method is that it allows for the treatment of the neurodegeneration associated with any demyelinating disease comprising the administration of any agent that inhibits DUSP6 expression and/or activity. Thus, the claims encompass an unreasonable number of pathologically distinct conditions and disorders, many of which have no nexus or association with the physiological function of DUSP6. The instant claims read upon a plurality of pathological conditions with different etiology, symptomology and courses of development and by the broadest reasonable interpretation read upon hereditary disorders, traumatic injury, infections, and developmental disorders and there is no evidence of record to indicate that any of these conditions are connected with DUSP6. Thus, a skilled artisan would not know how to treat these diseases by mere administration of a DUSP antagonist agent.

Furthermore, Claims 19-21 are so broad that they encompass the administration of any agent that inhibits DUSP6 expression and/or activity and are thus single means claims. MPEP 2164.08(a) defines a single means claim as a claim which covers every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be nonenabling for the scope of the claim in *In re Hyatt* , 708 F.2d 712, 218 USPQ 195

(Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property (i.e. inhibition of expression and/or activity), a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure or means for achieving the stated result while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claims are not commensurate in scope with the specification. Applicant should note that the claims are so broad as to encompass any agent that results in cell death of the cells to which it is applied, which is inhibition of the claims taken to the extreme.

While the skill level in the art is high, the level of predictability is low. As stated above, much unpredictability remains within the art as to the activity of DUSP6 in normal physiology and disease and currently there is no evidence of record to indicate a nexus or connection between DUSP6 and the etiology of any demyelinating disease.

The standard of an enabling disclosure is not the ability to make and test if the invention works but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling

disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

Examiner concludes that the instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. In the instant case, one of ordinary skill in the art would have to first identify DUSP6 activity and correlate said function with neurodegeneration associated with demyelinating diseases, then identify protein antagonists that inhibit the expression and/or activity of DUSP6 and, upon successful delivery across the BBB, demonstrate said antagonist was effective to treat the demyelinating disease, in order to practice the method as claimed. Such experimentation is not routine but constitutes undue experimentation in order to close the gaps between laboratory and clinical data.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is

(571)270-3057. The examiner can normally be reached on M-W and ALT F 5:30 to 3:30, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649